SA PHARMACY

FORMAL PATIENT CASE BASED PRESENTATION:

VANCOMYCIN & THERAPEUTIC DRUG MONITORING

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Government of South Australia

SA Health

CASE STUDY LEARNING OBJECTIVES

1. Discuss the Class, Mechanism of Action and Indications of Vancomycin
2. Importance of Therapeutic Drug Monitoring (TDM)
3. Discuss the Pharmacokinetic and Pharmacodynamic Parameters for Monitoring Vancomycin
4. Application of the SALHN Guideline – “Vancomycin Dosing and Monitoring Guideline for Adults”
5. Compare and Contrast Intermittent Bolus and Continuous Infusion of Vancomycin
6. Briefly discuss the progression of Vancomycin TDM – Vancomycin Area Under the Concentration-time Curve (AUC)/Minimum Inhibitory Concentration (MIC)

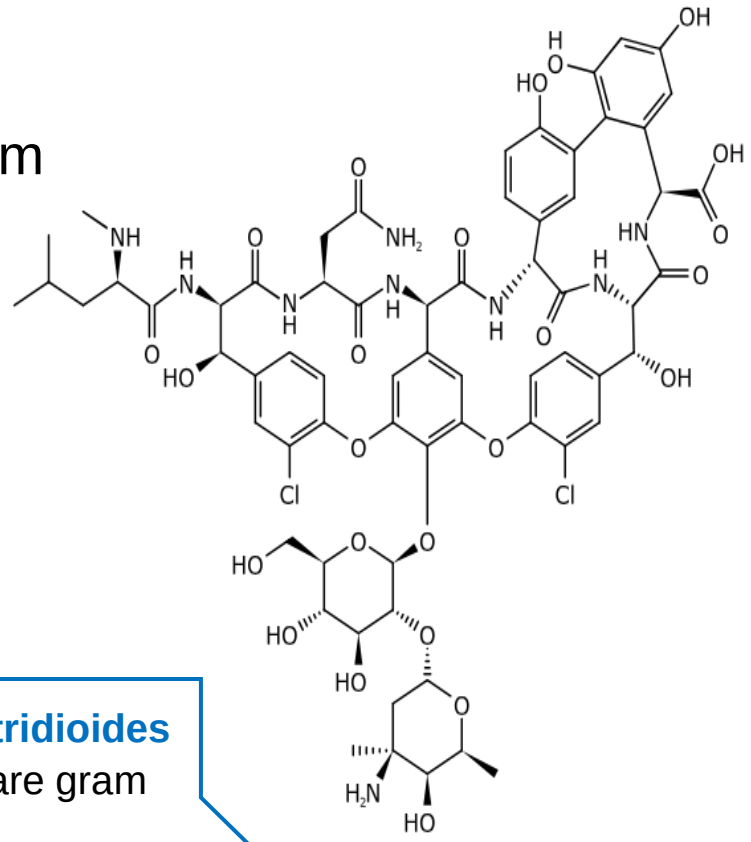
PHARMACIST COMPETENCY STANDARDS

- **Standard 3.1.2** Assess medication management practices and needs
- **Standard 3.1.3** Collaborate to develop a medication management strategy or plan
- **Standard 3.2.3** Dispense medicines (including compounded medicines) in consultation with the patient and/or prescriber
- **Standard 3.3.1** Undertake a clinical review
- **Standard 3.3.2** Apply clinical review findings to improve health outcomes
- **Standard 3.3.3** Document clinical review findings and changes in medication management
- **Standard 4.3.3** Encourage, influence and facilitate change

(National competency standards framework for Pharmacists in Australia, 2016)

BRIEF INTRODUCTION INTO VANCOMYCIN THERAPY

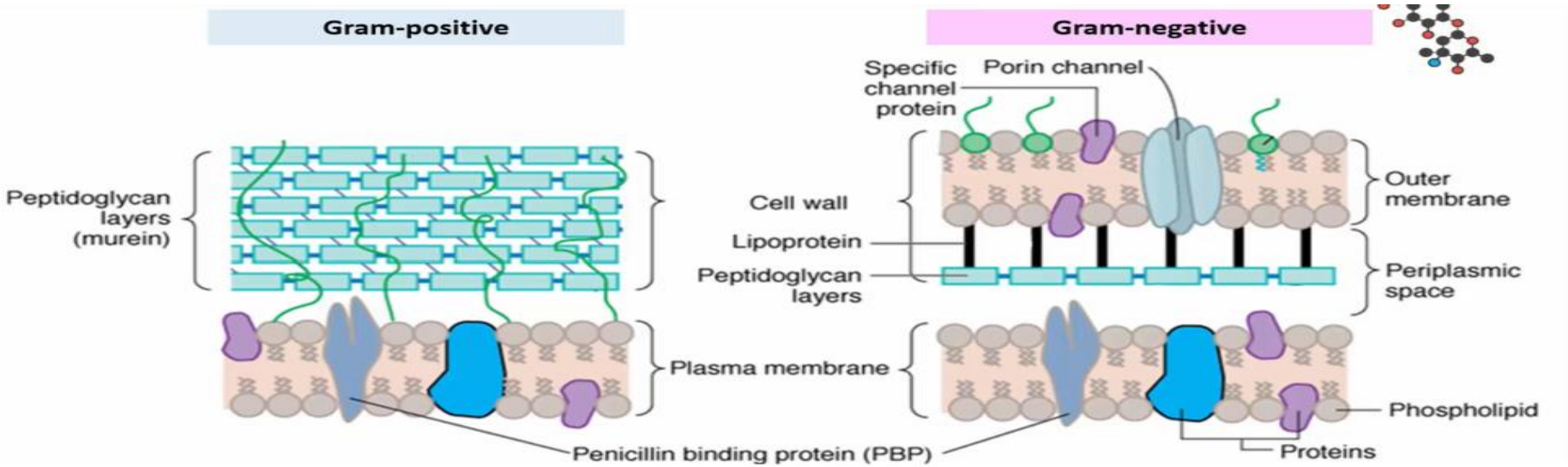
- **Class:** Glycopeptide antibiotic
- **Mechanism of action:** Bactericidal (kills bacteria)
  - Prevention of formation of cell wall synthesis in Gram positive bacteria
- **Indications:**
  - MRSA
  - Severe infections
  - Surgical prophylaxis
  - Antibacterial prophylaxis for endocarditis
  - Clostridioides Difficcile (oral)



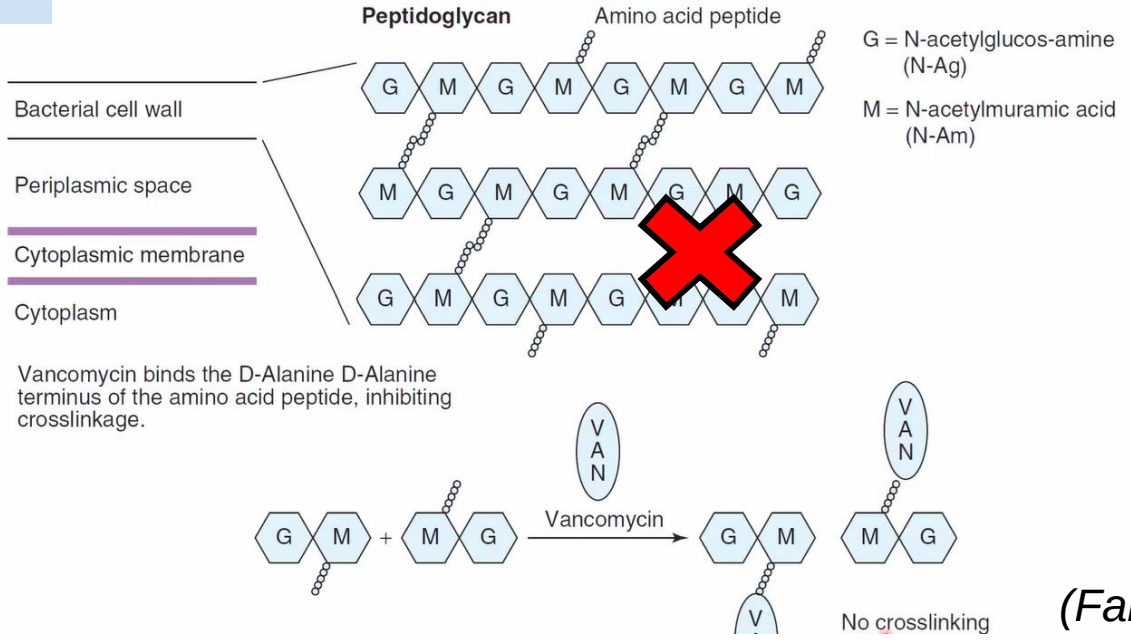
Vancomycin covers **Clostridioides difficile infection**, which are gram positive **anaerobes**

Gram-positive aerobes					Gram-negative aerobes				Anaerobe	Atypicals
Streptococci	Enterococci	VRE	MSSA	MRSA	H flu	M cat	EBC	PA	Bacteroides	Atypicals
+	+	–	+	+	–	–	–	–	–	–

(AMH , 2024)



Gram-positive



(FakhiRavari Alireza , 2019)

SA Medicines Formulary

SALHN Antimicrobial Restricted Guidelines

SA Health Antimicrobial Guidelines Admin

This guideline relates directly to the State Formulary Restrictions for antimicrobials. This page is updated regularly to reflect the current inclusions on the SA Medicines Formulary.

Vancomycin (IV)

A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z

Unrestricted Antimicrobials

No restrictions on use

Limited Release Antimicrobials

Refer to the specific agent for exemption criteria

(Infectious Disease approval is required if exemption criteria is not met. ICCU and NICU are exempt for all Limited Release antimicrobials)

Restricted Antimicrobials

Contact ID for approval code before use

(ICCU and NICU are allowed 48 hours supply after which time ID approval is required)

Vancomycin (IV)

Exemptions for use:

- Haematology/Oncology as per the febrile neutropenia guidelines;
- Surgical prophylaxis as per the SA Health guidelines allergic to penicillin or at high risk of Methicillin Resistant *Staphylococcus aureus* (MRSA) infection;
- Continuous Ambulatory Peritoneal Dialysis (CAPD) peritonitis involving Methicillin Resistant *Staphylococcus aureus* (MRSA) and coagulase-negative *Staphylococcus* (CNS);
- Empiric treatment of sepsis for 48 hours and then on ID advice.

If the intended indication for use is not listed above, ID approval is required

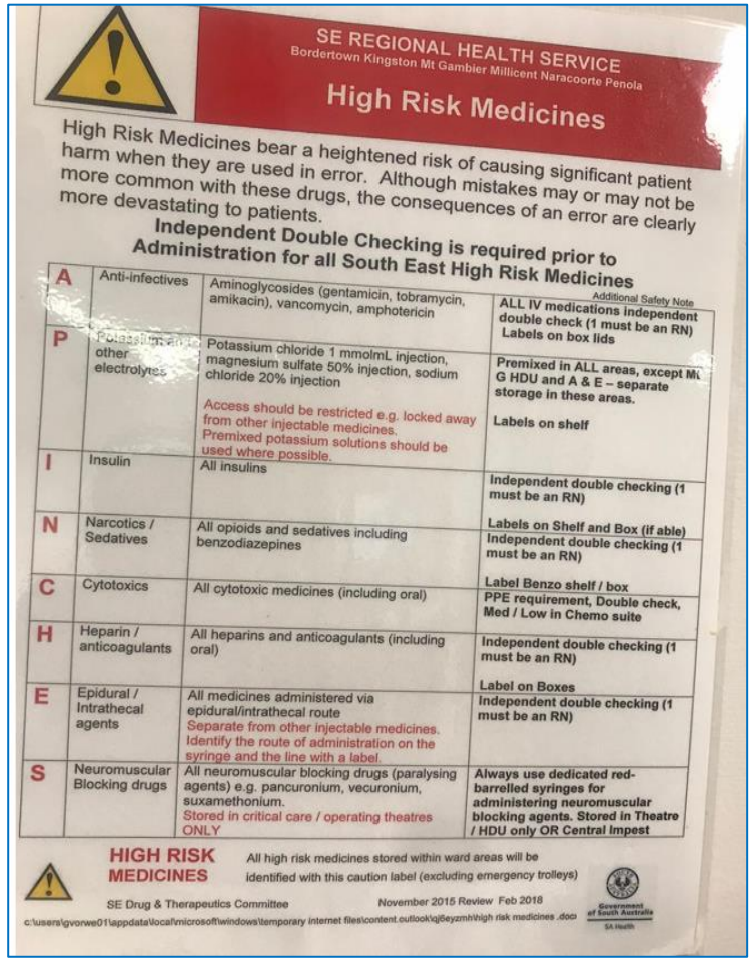
**dosing and monitoring as per the SALHN Vancomycin Dosing and Monitoring Guideline for Adults*

(SA formulary, 2024)

ADVERSE DRUG REACTIONS

WARNING

Extravasation may cause tissue necrosis.[1,2]
Vancomycin can cause severe infusion reactions including profound hypotension and vancomycin flushing (red man) syndrome. Do not infuse faster than the recommended rate.[1] Check your local guidelines.



SE REGIONAL HEALTH SERVICE
Bordertown Kingston Mt Gambier Millicent Naracoorte Penola

High Risk Medicines

High Risk Medicines bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients.

Independent Double Checking is required prior to Administration for all South East High Risk Medicines

			Additional Safety Note
A	Anti-infectives	Aminoglycosides (gentamicin, tobramycin, amikacin), vancomycin, amphotericin	ALL IV medications independent double check (1 must be an RN) Labels on box lids
P	Potassium and other electrolytes	Potassium chloride 1 mmol/mL injection, magnesium sulfate 50% injection, sodium chloride 20% injection Access should be restricted e.g. locked away from other injectable medicines. Premixed potassium solutions should be used where possible.	Premixed in ALL areas, except M G HDU and A & E – separate storage in these areas. Labels on shelf
I	Insulin	All insulins	Independent double checking (1 must be an RN) Labels on Shelf and Box (if able)
N	Narcotics / Sedatives	All opioids and sedatives including benzodiazepines	Independent double checking (1 must be an RN) Label Benzo shelf / box
C	Cytotoxics	All cytotoxic medicines (including oral)	PPE requirement, Double check, Med / Low in Chemo suite
H	Heparin / anticoagulants	All heparins and anticoagulants (including oral)	Independent double checking (1 must be an RN) Label on Boxes
E	Epidural / Intrathecal agents	All medicines administered via epidural/intrathecal route Separate from other injectable medicines. Identify the route of administration on the syringe and the line with a label.	Independent double checking (1 must be an RN)
S	Neuromuscular Blocking drugs	All neuromuscular blocking drugs (paralysing agents) e.g. pancuronium, vecuronium, suxamethonium. Stored in critical care / operating theatres ONLY	Always use dedicated red-barrelled syringes for administering neuromuscular blocking agents. Stored in Theatre / HDU only OR Central Impest

HIGH RISK MEDICINES All high risk medicines stored within ward areas will be identified with this caution label (excluding emergency trolleys)

SE Drug & Therapeutics Committee November 2015 Review Feb 2018

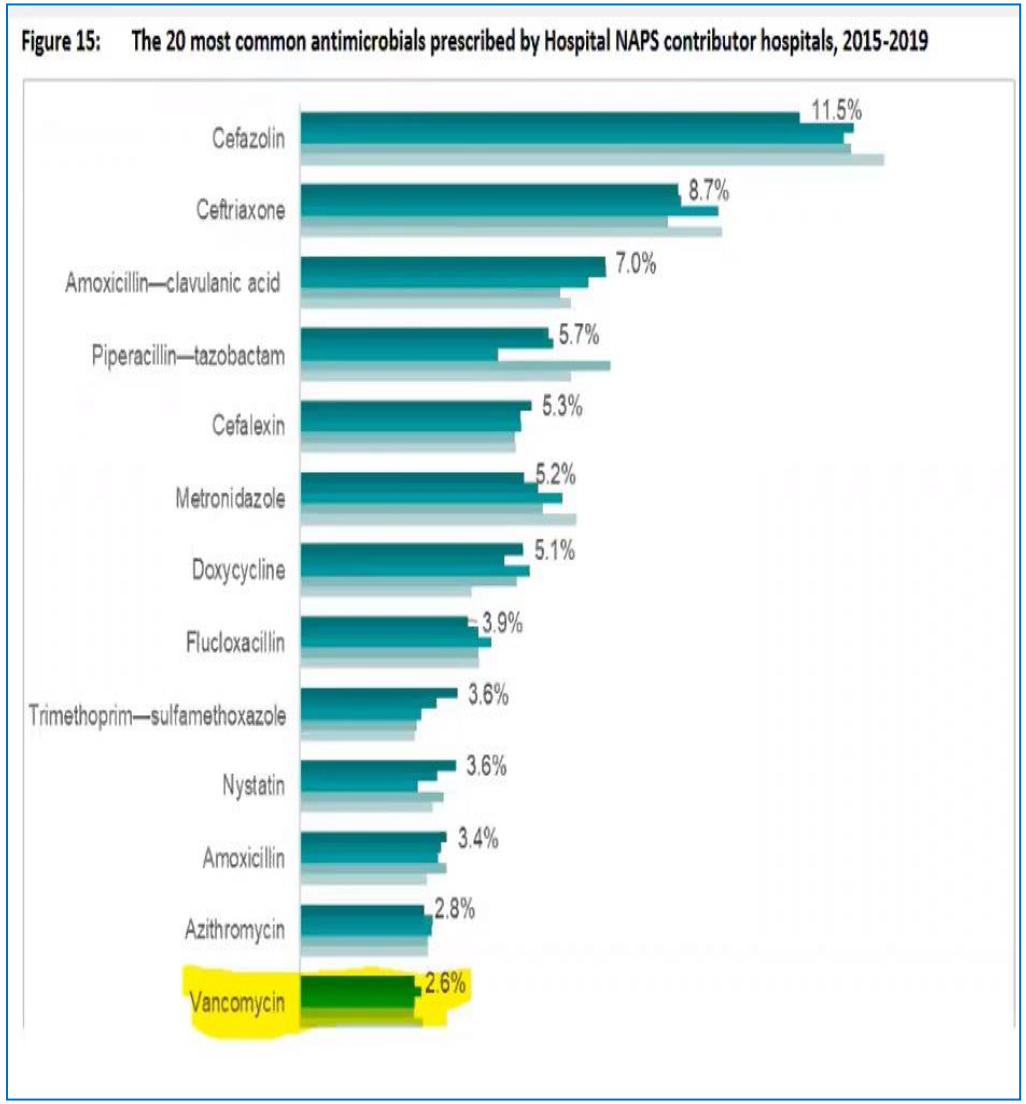
c:\users\gvorwe01\appdata\local\microsoft\windows\temporary internet files\content.outlook\qj6eyzmh\high risk medicines .doc

Government of South Australia SA Health

(SA Health, 2015)

- **Red man syndrome:** Associated with rate of infusion
- **Neutropenia:** Occurs in 12% of patients with prolonged use of Vancomycin
- **Ototoxicity:** Uncommon, typically related to older formulations
- **Significant skin reactions:** Includes uncomplicated rashes, bullous eruptions, SJS/TEN and DRESS
- **Nephrotoxicity:** More likely with high doses and prolonged therapy
- **Acute Kidney Injury:** Reported in 8% of cases with trough-based dosing compared to 2% with AUC based dosing

CURRENT USE OF VANCOMYCIN



ACSQHC, 2021

In Australian Hospitals:

- 2-3 out of 100 in patients are administered Vancomycin

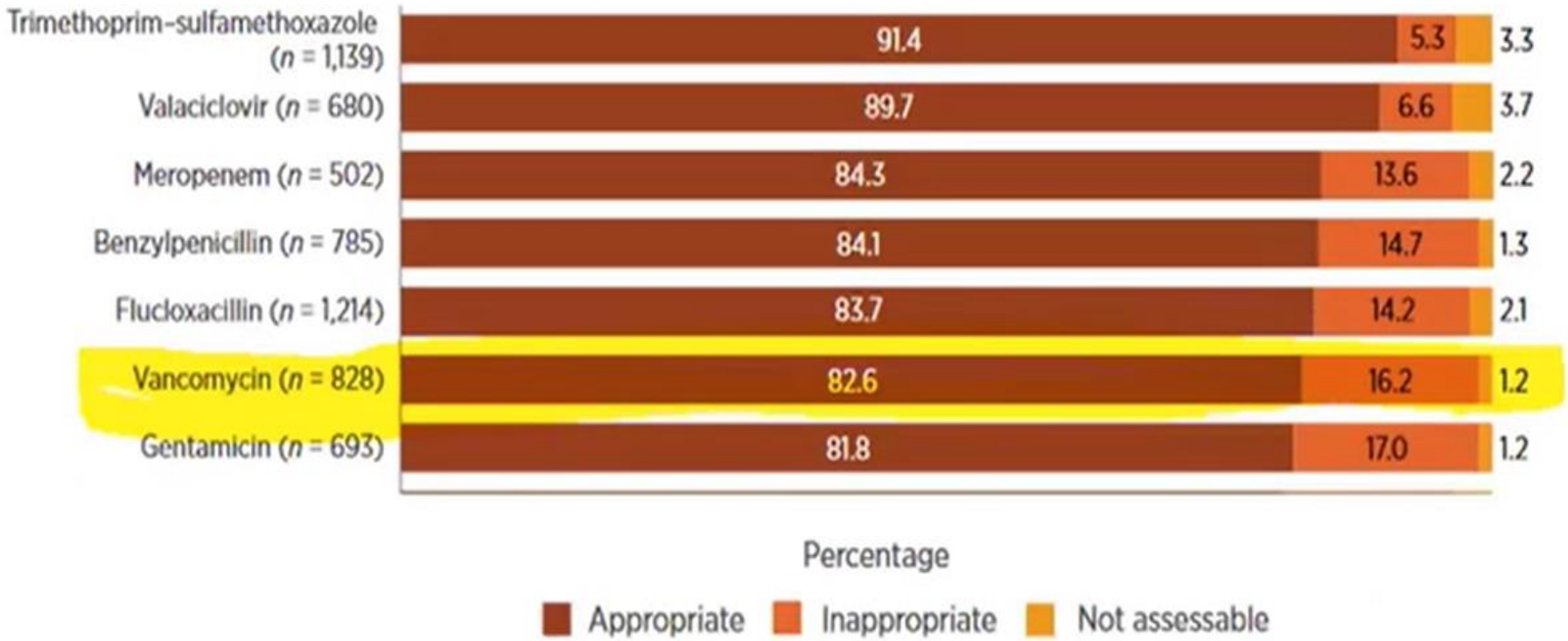
Top 3 indications:

- Bacteraemia
- Sepsis
- Surgical Prophylaxis

APPROPRIATENESS FOR PRESCRIBING

- **Poorly prescribed ~2 in 10 prescribing are not appropriate**

Figure 3.8: Appropriateness of prescribing for the most commonly prescribed antimicrobials in Hospital NAPS contributor hospitals, 2019



ACSQHC, 2021

WHY DO PHARMACISTS NEED TO BE EXPERTS?

MRSA rate of mortality

What is the 30-day mortality of MRSA bloodstream infection in Australia?

A. 1 - 10 %

B. 10 - 20%

C. 20 - 30 %

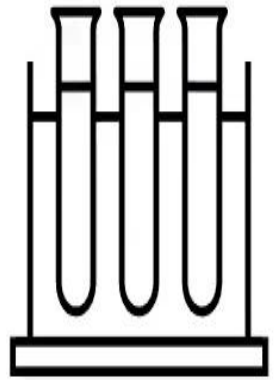
D. 30 - 40 %

20 - 30% Adults

Specimen Information

Order:	Culture Blood	Collect Date/Time:	12/07/2021 12:45:00
Growth Ind:	See Report	Last Update Date/Time:	15/07/2021 08:52:18
Status:	Completed	Testing Site:	CHW MYLA
Source:	Blood	Freetext Source:	
Body Site:		Accession #:	000002021193000373

	Methicillin-Resistant Staphylococcus aureus
Drug	MIC Interp
Cefazolin	R
Methicillin	R
Penicillin	R
Vancomycin	S

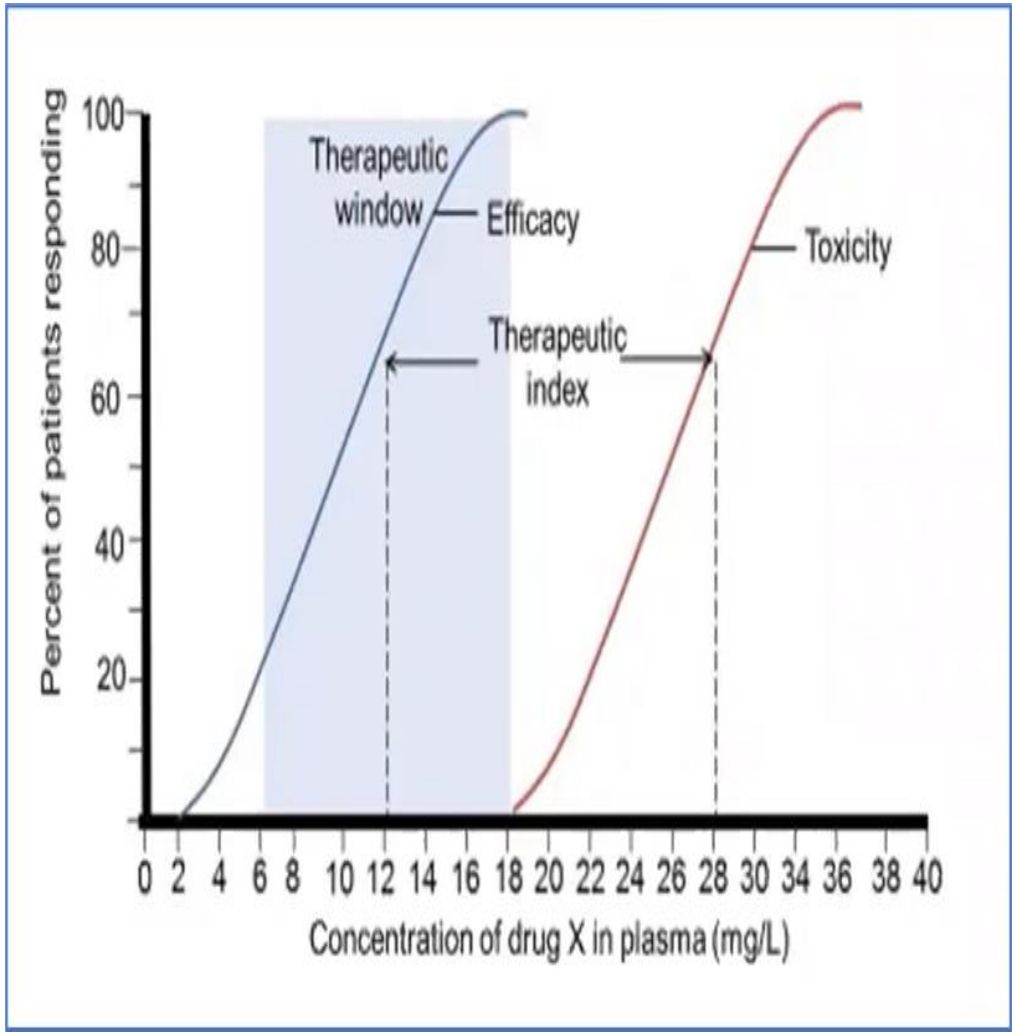


(SA Health, 2015)

IMPORTANCE OF THERAPEUTIC DRUG MONITORING

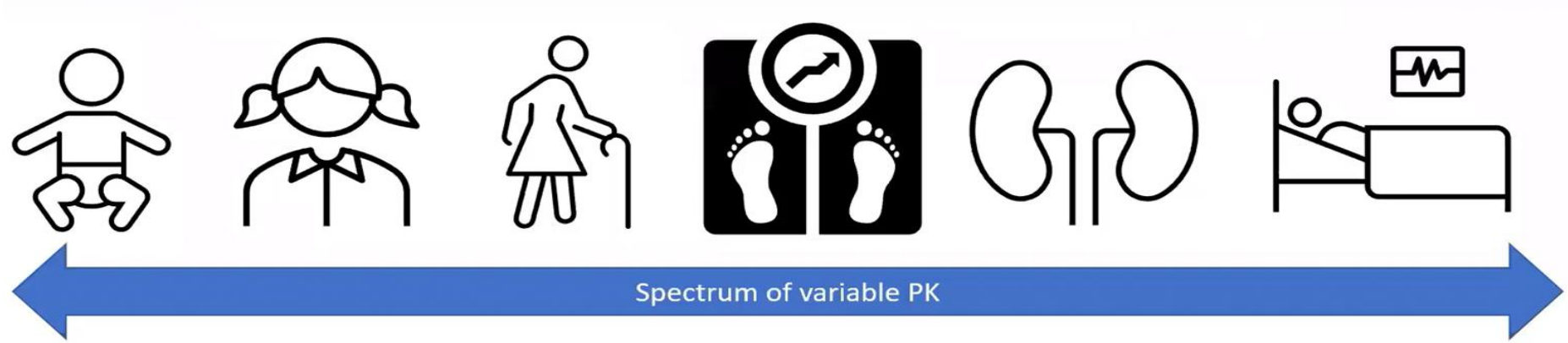
Most common medicines have a relatively wide therapeutic index (‘safety margin’).

1. Vancomycin has a narrow therapeutic index
2. Established relationship between plasma concentration and beneficial/harmful effects
3. Therapeutic or toxic effects that are difficult to measure directly– Supratherapeutic or subtherapeutic
4. Significant variability between patients
5. Results interpretable and actionable – effect on clinical outcome



(Lodise T CID, 2009)

VARIABILITY IN PHARMACOKINETICS



PHARMACOKINETIC PROPERTIES

Absorption:
- Oral bioavailability: Nil
- Intraperitoneal bioavailability: 40-60%

Distribution:
- Protein binding: 55% (normal renal function)
- Volume of distribution: ~0.7 L/kg (varies)
  - Distributes poorly into CNS and adipose tissue

Metabolism:
- No apparent Metabolism

Excretion:
- Predominantly renally eliminated 40-100%

Half Life:
- Normal renal function 4-6 hours (adult)

(Uptodate, 2024)

- **Volume of Distribution:** ~0.7 L/kg (varies)
  - **Hydrophilic drug – low Vd**
  - **Protein binding – Main carrier Albumin**
- **Predominantly renally cleared:** Adjust based on patient's renal function
  - **Acute Kidney Injury**
  - **Chronic Kidney Disease**
  - **Augmented renal clearance**
- **Half-life (t ½) for adults:** 4 - 6 hours
  - **Half life depends on renal function**
  - **Loading dose to reach steady state faster**

CLINICAL APPLICATION OF VANCOMYCIN BASED ON SALHN GUIDELINES

- **Vancomycin loading dose**
  - Standard 25 mg/kg of actual body weight irrespective of CrCl
- **Initial maintenance dose**
  - Influenced by patient's CrCl and actual body weight, dosing for up to 48 hrs
- **Monitoring of Vancomycin level**
  - Based on patient's CrCl and trough concentration after initial maintenance
- **Dose adjustment for intermittent infusions**
  - Determined by trough concentration
- **Conversion from intermittent to continuous infusion**
  - Convert to 24 hour dose and commonly reduced by 20%

(SALHN Infectious Diseases , 2024)

PATIENT CASE STUDY

SA PHARMACY – PRIVATE WARD, MOUNT GAMBIER HOSPITAL

ADMISSION DATE 24/02/2024 – DISCHARGED 02/03/2024

CASE INFORMATION

- **Presenting Complaint:** Mr Bob Smith (anonymous), 91y male was down transferred from FMC to MGH after being admitted for an eroded right PPM pocket removal and left PPM replacement with leadless pacemaker (Micra – Medtronic pacemaker)
  - Loading dose and initial maintenance dose administered at FMC
  - GMT @ MGH and continued Vancomycin upon admission on 24/02/24

- **Relevant findings from investigations:**
  - Gram +ve Bacilli
  - Obtained on 16/02/24 @FMC

RESULT:

24-045-05256

Microbiology

Procedure: Culture Swab []
Source: Swab
Accession: 24-045-05256
Collected: 14-Feb-24 11:30

FINAL REPORT
Verified Date/Time: 16-Feb-24 09:28
+++ skin flora

MICROSCOPY
Verified Date/Time: 14-Feb-24 21:43
No polymorphs
+ Gram positive bacilli

CASE STUDY – PATIENT INFORMATION

Bob Smith (Anonymous patient)

Gender: Male
Age: 91 years old (07/01/1933)
Background: Lives at home alone in Mount Gambier
SHx: Supportive daughter lives nearby. Independent with ADLs. Nil smoker/drinker. Nil recent travel
Body measurements:

- **Height:** 187 cm (13/02/2024)
- **Weight:** 120 kg (13/02/2024)
- **BMI:** 34.3 kg/m^2 **(Obese)**

- **PMHx:** Coronary artery disease, Gastro-oesophageal reflux disease, Hypertension, Paroxysmal Atrial Fibrillation (on Warfarin), Depression, and Urinary Incontinence
- **Allergies:** **Cefalexin (Itching)** and opioid-like analgesics (Hallucination)
- **Medication Hx:** Atorvastatin 40mg mane, Duloxetine 60mg mane, Dutasteride/Tamsulosin 500/40mcg nocte, Isosorbide Mononitrate SR 60mg nocte, Furosemide 40mg mane and 20mg midday, Oxybutynin 5mg nocte, Pantoprazole 40mg mane, Sotalol 80mg BD, GTN 400 mcg 1-2 sprays Q5M PRN, and Warfarin 5 mg in the evening.
- **Past Surgical Hx:** Bilateral Total Knee Replacement, Left Total Hip Replacement, and Permanent Pacemaker for complete heart block (2010 @FMC)
- **Care Providers:** Port MacDonnell Pharmacy, Ferrers Medical Clinic, Heart & Vascular (Dr Lahiri – Cardiologist), Flinders Medical Centre and Mount Gambier Hospital

CASE STUDY – VANCOMYCIN TREATMENT INFORMATION

- **Investigations:** Blood cultures unremarkable. Culture swab, gram positive Bacilli confirmed on 16/02/24.
  - No MRSA detected.
- **ID approval:** ID Consult 2 days prior to investigation report @ FMC recommended to treat as pacemaker pocket site erosion/infection rather than bacteraemia/ infective endocarditis with total of 14 days IV Vancomycin.
  - IV Vancomycin to commence at beginning of leadless PPM insertion
  - Start 21/2/24 – end 06/03/24
- **Target therapeutic trough level:** 15.0 – 20.0mg/L
- **Patient clinical status:** Afebrile and observations are stable
- **Relevant pathology results:**
  - **SeCr:** 91 micromole/L (19/02/2024)
  - **CrCl:** 54 mL/min (19/02/2024)

Cardiac implantable electronic device pocket infection

For empirical therapy of **uncomplicated** pocket infection, after taking three sets of blood for culture (from separate venipuncture sites), use:

vancomycin intravenously; see Principles of vancomycin use for dosage and principles of use.

Modify therapy based on the results of culture and susceptibility testing.

Continue antibiotic therapy after the device and leads are removed. For uncomplicated infections, 2 weeks of therapy is usually sufficient, provided the device has been completely removed and local soft tissue infection has resolved. If the cardiac implantable electronic device is not removed, seek expert advice for antibiotic therapy choice and duration.

(Therapeutic Guidelines, 2024)

CASE STUDY – LOADING DOSE

Table 1: Vancomycin loading dose determination

Loading doses are recommended for patients requiring rapid attainment of target concentration. Dose stratified based on 25mg/kg of actual body weight.

Actual Body Weight (kg)	Loading Dose (grams)
40-44kg	1g
45-54kg	1.25g
55-64kg	1.5g
65-79kg	2g
80-119kg	2.5g
>120kg and CrCl <59ml/min	2.5g
>120kg and CrCl >60ml/min	3g (maximum)

(AMS Pharmacist/ Infectious Diseases, 2020)

Patient's loading Dose - 2.5g completed @ FMC 21/02/24 @07:46AM

Was this an appropriate loading dose?

- 25 mg/kg = 25 mg/kg x 120 kg = 3000mg = 3g (maximum), or
- Actual Body Weight (kg) – 120kg (>120kg category) & CrCl = 54 mL/min (<59 mL/min category), therefore 2.5g loading dose at FMC

What would your recommendation be?

- Loading administered at FMC is correct

CASE STUDY – INITIAL MAINTENANCE DOSE

(AMS Pharmacist/ Infectious Diseases, 2020)

Table 2: Recommended initial maintenance dose (for up to 48 hours)

Based on calculated creatinine clearance (CrCl); Do not use eGFR for dosing as this is not accurate for extremes of body size; Start maintenance dose 12 hours after the loading dose (if giving 12-hourly) or 24 hours after the loading dose (if giving 24-hourly)

Actual Body Weight (Contact ID if <40kg)	Creatinine Clearance (mL/min)			
	CrCl > 60	CrCl 40-59	CrCl 20-39	CrCl <20 (Contact ID)
40-49kg	750mg 12-hourly	750mg 12-hourly	750mg 24-hourly	750mg*
50-64kg	1g 12-hourly	750mg 12-hourly	1g 24-hourly	1g*
65-78kg	1.25g 12-hourly	1g 12-hourly	1.25g 24-hourly	1.25g*
79-92kg	1.5g 12-hourly	1.25g 12-hourly	1.5g 24-hourly	1.5g*
93-107kg	1.75g 12-hourly	1.25g 12-hourly	1.75g 24-hourly	1.75g*
>108kg	2g 12-hourly	1.5g 12-hourly	2g 24-hourly	2g*

**Check initial level 24 hours after initial loading dose; Re-dose only when level is <20mg/L; Repeat levels every 1-2 days*

Patient's initial maintenance dose 1.5 g IV BD – FMC 21/02/24 @8:35PM

Was this an appropriate treatment regime?

- Actual Body Weight 120 kg (>108kg) & CrCl 54 mL/min (40- 59 mL/min), therefore 1.5g 12-hourly at FMC

What would your recommendation be?

- Initial maintenance doses administered in FMC are correct

CASE STUDY – MONITORING OF VANCOMYCIN LEVEL

(AMS Pharmacist/ Infectious Diseases, 2020)

Table 3: Monitoring of vancomycin level

Trough concentration should be obtained approximately one hour before the next dose is due.

Creatinine Clearance (mL/min)		
CrCl >40	**CrCl 20-39**	**CrCl <20**
Check level **before the fourth dose** *(including loading dose if given)*	Check level **before the third dose** *(including loading dose if given)*	Check level 24 hours after loading dose

NOTE: *For each dose and/or frequency alteration during therapy, obtain a trough level as per the table above after commencement of the new dose/frequency and continue to adjust as necessary.*

Time	Dose Administered	TDM Concentration	Serum Creatinine
21/02/2024 @7:46AM FMC	2.5g – Loading Dose		
21/02/2024 @8:35PM FMC	1.5g – Initial maintenance dosing		
22/02/2024 @8:05AM FMC	1.5g – Initial maintenance dosing		**85micromoles/L @06:07AM**
22/02/2024 @8:15PM FMC	1.5g – Initial maintenance dosing		
23/02/2024 @8:26AM FMC	1.5g	**19.2mg/L @8AM**	**73micromoles/L @7:59AM**

Trough concentration - 19.2mg/L at FMC 23/2/24 @8AM before 5th dose

When should the timing of trough level be?

- CrCl 54mL/min (>40mL/min) – Before the 4th dose (loading dose inclusive)
- Recommended to take before 4th dose – level taken later than recommended

What would your recommendation be?

- Prefer correct trough level timing – trough reading may be underestimated

CASE STUDY – DOSE ADJUSTMENT FOR INTERMITTENT INFUSIONS

Table 4: Dosage adjustment for intermittent infusions based on trough concentration

Trough Concentration (mg/L)	Creatinine Clearance (mL/min)		
	CrCl >40	CrCl 20-39	CrCl <20
< 10mg/L	Increase **total daily dose** by 1g *(seek ID advice if daily dose >4g/day)*	Increase **total daily dose** by 500mg	Re-dose when trough concentration <20mg/L
10-14mg/L	Increase **total daily dose** by 500mg	Increase **total daily dose** by 250mg	
15-20mg/L	**IN TARGET RANGE- no change required** Repeat trough levels every 48 hours until stable; then repeat **twice** weekly if renal function remains stable.		
21-25mg/L	**Reduce each dose by 250mg**		
> 25mg/L	**HOLD dose for 24 hours** Re-check level and recommence at reduced dose when trough level is <20mg/L; Review renal function		

(AMS Pharmacist/ Infectious Diseases, 2020)

Time	Dose Administered	TDM Concentration	Serum Creatinine
23/02/2024 @8:26AM FMC	1.5g	**19.2mg/L @8AM**	**73micromoles/L @7:59AM**
23/02/2024 @8:41PM FMC	1.5g		
24/02/2024 @7:51AM TRANSFER TO MGH	1.5g		
24/02/2025 @8:41PM	1.5g	**26.4mg/L @8:01PM**	
25/02/2024 @AM	HELD		**74micromoles/L @8:17AM**

Trough concentration – 26.4mg/L at MGH 24/02/2025 @8.01PM before 4th dose

Was this an appropriate decision to hold treatment?

- Appropriate timing of level as 24 hours from previous level
- CrCl >40mL/min – 67mL/min on 23/02/2024 @7:59AM
- Trough concentration >25mg/L – 26.4mg/L on 24/02/2024 @8:01PM. Dose held for 24 hours

What would your recommendation be? Hold dose for 24 hours

CASE STUDY – DOSE ADJUSTMENT FOR INTERMITTENT INFUSIONS

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(AMS Pharmacist/ Infectious Diseases, 2020)

Time	Dose Administered	TDM Concentration	Serum Creatinine
24/02/2024 @7:51AM TRANSFER TO MGH	1.5g		
24/02/2025 @8:41PM	1.5g	**26.4mg/L @8:01PM**	
25/02/2024 @AM	HELD		**74micromoles/L @8:17AM**
25/02/2024 @PM	HELD	**17.8mg/L @8:30PM**	
26/02/2024 @7:57AM	1.25g		

Re-check level and recommence when trough level <20mg/L

Was this an appropriate decision to recommence treatment regime?

- Dose held for 24 hours
- Trough concentration <20mg/L – 17.8mg/L on 25/2/24 @08:30PM
- CrCl >40mL/min – 66mL/min on 25/02/2024 @08:17AM

What would your recommendation be? Previous trough level ~25mg/L – 26.4mg/L on 24/2/24 @08:01PM

- Reduced each dose by 250mg – 1.25g on 26/02/2024 @7.57AM

CASE STUDY – DOSE ADJUSTMENT FOR INTERMITTENT INFUSIONS

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15-20mg/L	**IN TARGET RANGE- no change required** Repeat trough levels every 48 hours until stable; then repeat **twice** weekly if renal function remains stable.		
21-25mg/L	**Reduce each dose by 250mg**		
> 25mg/L	**HOLD dose for 24 hours** Re-check level and recommence at reduced dose when trough level is <20mg/L; Review renal function		

(AMS Pharmacist/ Infectious Diseases, 2020)

Time	Dose Administered	TDM Concentration	Serum Creatinine
25/02/2024 @PM	1.5g - HELD	**17.8mg/L @8:30PM**	
26/02/2024 @7:57AM	1.25g		
26/02/2024 @8:26PM	1.25g		
27/02/2024 @9:32AM	1.25g		**80micromoles/L @10AM**
27/02/2024 @8:34PM	1.25g	**22.8mg/L @8:13PM**	

Re-check levels for adjusted dose and further dose adjust if necessary

What should we do in this scenario?

- CrCl > 40mg/mL (CrCl = 61 mL/min on 27/02/2024 @10:00AM
- Trough concentration 21-25mg/L (22.8mg/L on 27/02/2024 @08:13PM before 4th dose)

What would be your recommendation?

- Further reduce each dose by 250mg - new dose of Vancomycin is 1g IV BD

CASE STUDY – VANCOMYCIN TROUGH LEVELS GET TRICKY!

Time	Dose Administered	TDM Concentration	Serum Creatinine
27/02/2024 @8:34PM	**1.25g**	**22.8mg/L @8:13PM**	
28/02/2024 @8:10AM	**1.25g**		**71micromoles/L @8:56AM**
28/02/2024 @8:10PM	**1g**		
29/02/2024 @8:37AM	**1g**	**22mg/L @8:04AM**	**75micromoles/L @8:04AM**
29/02/2024 @8:25PM	**1g**	**20.8mg/L @7:21PM**	

Delay in dose adjustment after reading on 27/2/24 @08:13PM until 3rd dose!

What are the consequences of the delayed dose adjustment?

- Supratherapeutic dose administered on 27th PM & 28th AM – increased risk of toxicity
- Trough readings on 29/2/24 is expected to be high due to delayed dose adjustment

What would be your recommendation?

- Dose adjustments must be made as soon as possible!
- After delayed dose adjustment best indication of trough level is prior to 4th AM dose of 1g on 1/3/24
- Not tremendously concerned with 20.8mg/L (target 15-20mg/L) as trough reading is early

PROGRESS NOTE:

INTERVAL HISTORY:

- **Interval History**

General Medicine RMO [redacted]

Discussion with private ward TL [redacted] and pharmacist Yusri re: patient's vancomycin Baxter pump
Patient unlikely to be able to be discharged on Baxter pump tomorrow as planned
Vancomycin level today: 22.0 (supra-therapeutic); confirmed with TL that this was definitely taken as a trough level prior to his 8am dose this morning; however this level shouldn't have been taken as next level wasn't due

PROGRESS NOTE:
INTERVAL HISTORY:

- **Interval History**

Medical review - [redacted]

ATSP: Vancomycin level

Vanc level mild supratherapeutic 20.8 (aim 15-20)
- acknowledge vagueness of SA Health Guideline when level between 20-21

Plan
1) Decrease Vanc dose to 750mg BD from this AM
2) Continue monitoring trough level

The clinician:

- Utilised early level - 20.8 to make clinical judgement
- Acknowledged vagueness of CALHN guideline when level slightly Vancomycin level
- Recommended dose adjustment in accordance with SA Health guideline
- Used best clinical judgement to ensure patient safety

CASE STUDY – CONTINUOUS INFUSION CONVERSION

Patients for administration of vancomycin out of hospital (e.g. with Hospital in the Home (H@H)):

- Patients to receive vancomycin via H@H administration will preferably have **two** consecutive vancomycin concentrations within target range **prior** todischarge.
- A dose reduction of approximately 20% is required when converting from intermittent to 24-hour continuous infusion.
- Please ensure treating team to provide H@H staff with appropriate signed pathology request forms (i.e. tick the rule 3 exemption to allow for continued use).
- A vancomycin concentration is to be taken 24 hours post-commencement of continuous infusion (target range 20-25mg/L).
- Monitoring of vancomycin concentrations and urea & creatinine will be required **twice weekly** until stable then weekly for patients receiving vancomycin via H@H.
- Infectious Diseases H@H registrar is responsible for amending vancomycin dosage and determining frequency of monitoring for patients being administered vancomycin by H@H.

(AMS Pharmacist/ Infectious Diseases, 2020)

What would be your dose conversion recommendation?

- **Baxter pump requested prior to clinician dose reduction**
- **1g IV 12 hourly** intermittent dosing = **2g/ 24-hour** continuous infusion
- **Dose reduction of 20%** is appropriate due to ambiguity with elevated trough level
- Furthermore, conversion to continuous infusion can increase levels by 20%
- **2g/ 24 hours x 0.8 = 1.6g/ 24 hours** continuous infusion
- Baxter pump ordered – 1.6g/ 24 hours to facilitate **discharge prior to weekend**
- Commence Baxter continuous infusion immediately **after intermittent** dose given

CASE STUDY – CONTINUOUS INFUSION

Key points of TDM of Vancomycin continuous infusion:

- Therapeutic range for non-CNS infections (including bacteraemia and endocarditis) is **20-25 mg/L**
- A Vancomycin concentration needs to be taken once a steady state has been reached, **16 hrs after initiation** of continuous infusion
- Monitor levels **every 24 hrs** till recommended therapeutic concentrations have been recorded over **2 consecutive days**. Monitor levels **every 48 hrs** thereafter
- Continuous infusion is **well-tolerated** and require **less blood sampling** compared to intermittent infusion

(AMS Pharmacist/ Infectious Diseases, 2020)

CASE STUDY – TDM OF CONTINUOUS INFUSION

Time	Dose Administered	TDM Concentration	Serum Creatinine
29/02/2024 @8:37AM	**1g**	**22mg/L @8:04AM**	**75 micromoles/L @8:04AM**
29/02/2024 @8:25PM	**1g**	**20.8mg/L @7:21PM**	
01/02/2024 @8:35AM	**750mg**		
01/02/2024 @12:40PM	**1.6g/ 24-hour infusion**		
02/03/2024 @11:47AM & DISCHARGED	**1.6g/ 24-hour infusion**	**22.7mg/L @5:56PM**	

Was this an appropriate timing of initial level following commencement?

- Continuous infusion commenced on 01/02/2024 at 12:40PM
- Vancomycin concentration taken on 02/03/2024 at 5:56PM
- Timing interval ~29 hours

What would your recommendation be?

- Initial steady state level 02/03/2024 at 4:40AM (16 hours post commencement)
- Check level as soon as steady state reached to assess toxicity/therapeutic effect
- Adjust dose as necessary

CASE STUDY – TDM OF CONTINUOUS INFUSION

Time	Dose Administered	TDM Concentration	Serum Creatinine
03/03/2024 @HOME	**1.6g/ 24-hour infusion**	**Missed reading**	
04/03/2024 @HOME	**1.6g/ 24-hour infusion**	**17.9mg/L @11AM**	**79micromoles/L @11AM**
5/03/2024 – 06/03/2024 @HOME	**1.6g/ 24-hour infusion**	**Not available**	

Doctor discharge plan (02/03/2024) - outpatient monitoring

Vancomycin 1.6g IV Infusion every 24 hours until 06/03/24 through PICC line

- DOSE CHANGE:

Warfarin increased to 8mg daily until GP review

3. Please get a blood test on Monday 4/03/2024 using the form provided (INR, Vancomycin level, FBC/EUC)

4. Please follow up with your GP on 4/03/2024. GP to kindly:

- review progress
- chase INR and titrate warfarin accordingly
- chase vancomycin level. Target level: *20.0 - 25.0*
  - no action required if therapeutic or subtherapeutic
  - if vancomycin level > 25, please send John back to Mount Gambier Hospital as his baxter pump dose will need to be reduced
- PICC line and waterproof dressing can both be removed after completion of antibiotics on 6/3/2024

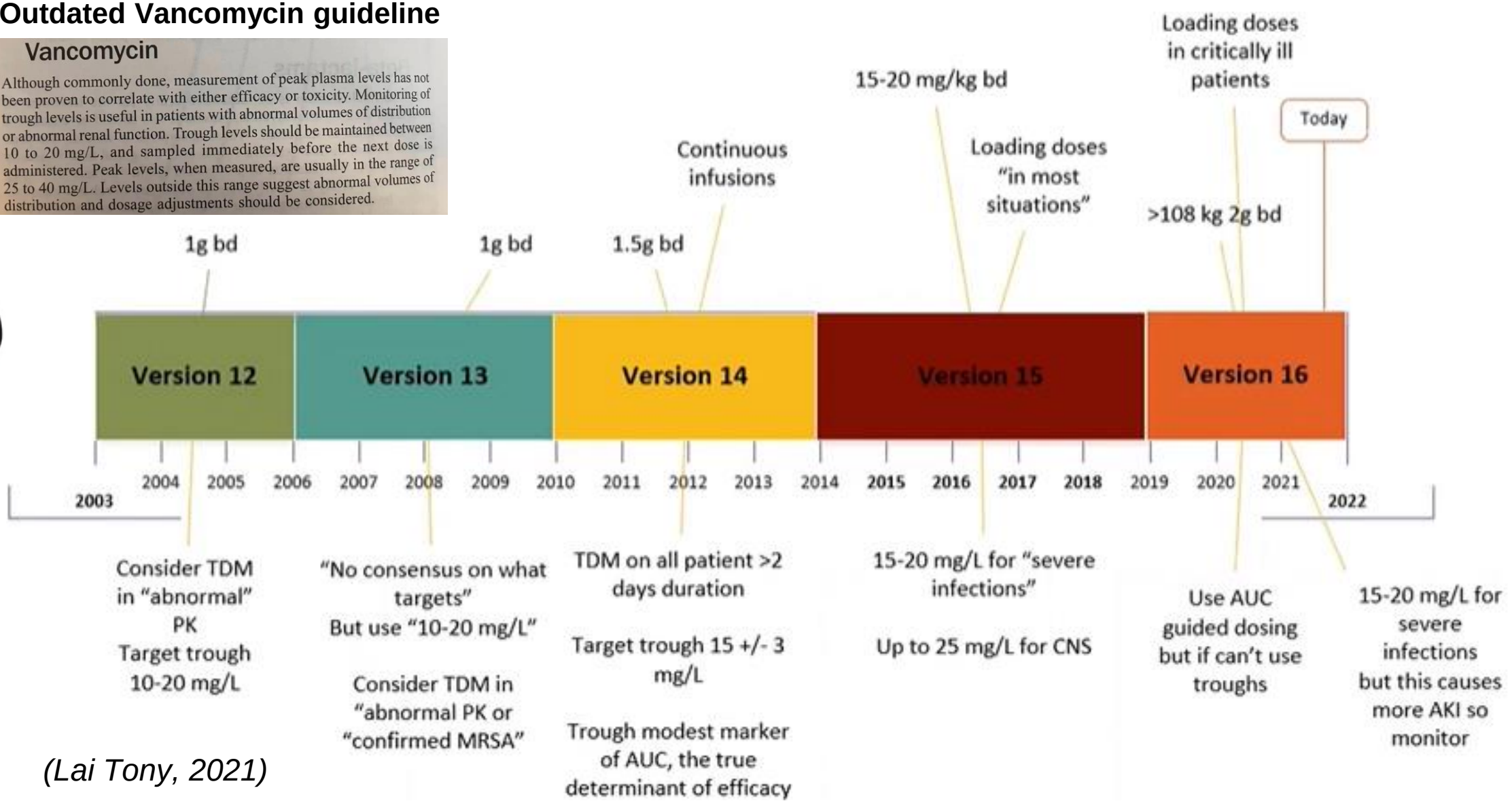
PROGRESSION OF VANCOMYCIN THERAPEUTIC DRUG MONITORING:

Therapeutic Guidelines

Outdated Vancomycin guideline

Vancomycin

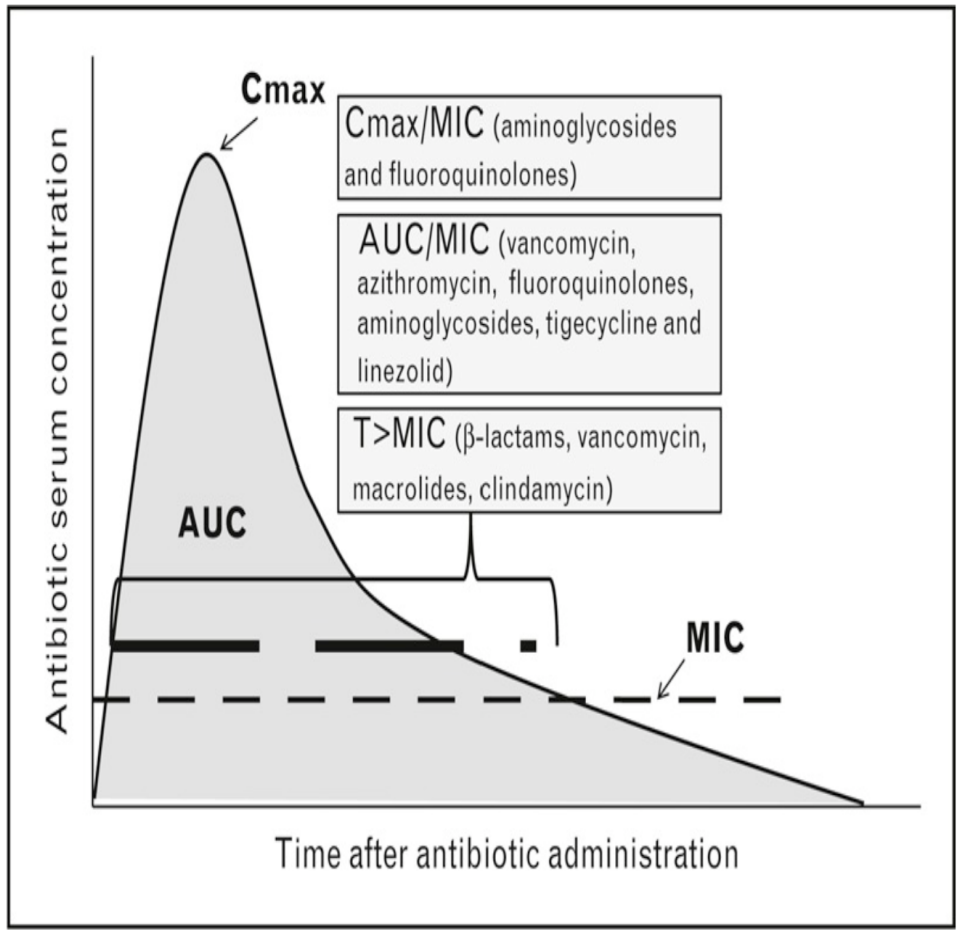
Although commonly done, measurement of peak plasma levels has not been proven to correlate with either efficacy or toxicity. Monitoring of trough levels is useful in patients with abnormal volumes of distribution or abnormal renal function. Trough levels should be maintained between 10 to 20 mg/L, and sampled immediately before the next dose is administered. Peak levels, when measured, are usually in the range of 25 to 40 mg/L. Levels outside this range suggest abnormal volumes of distribution and dosage adjustments should be considered.



(Lai Tony, 2021)

PROGRESSION OF VANCOMYCIN THERAPEUTIC DRUG MONITORING:

Area Under the concentration-time Curve (AUC)/Minimum Inhibitory Concentration (MIC)

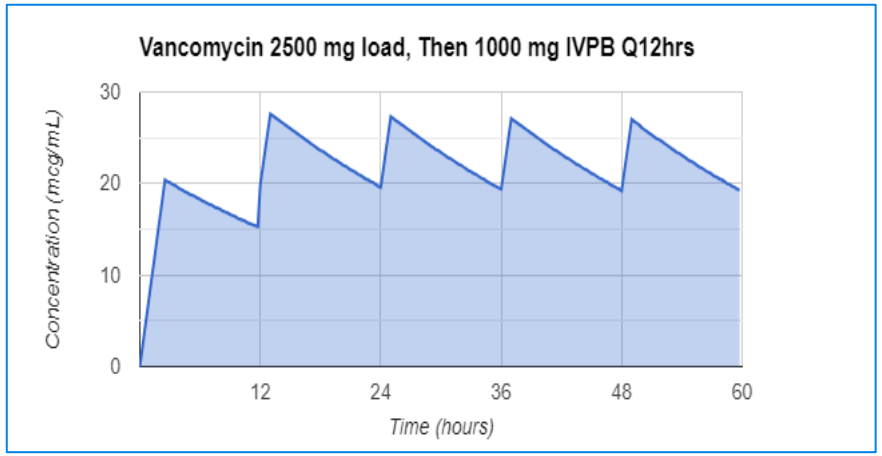


(Lai Tony, 2021)

- AUC/MIC is the best method of Vancomycin monitoring
- Antimicrobial activity are a mixture of time dependent and moderate persistent effects
- Best determinant of efficacy
- Reduced risk of adverse side effects
- Allows optimal dosage of drug administration
- A 24-hour AUC/MIC of 400 or more is the target for best clinical outcomes

PROGRESSION OF VANCOMYCIN THERAPEUTIC DRUG MONITORING:

BAYESIAN METHOD



Compare Dosing Options

Dose	Frequency	AUC/MIC	Peak	Trough	
		Q12hr			
1000 mg (8mg/kg)	Q12hr	541	26.6	18.9	
1250 mg (10mg/kg)	Q12hr	676	33	23.8	Select
1500 mg (12mg/kg)	Q12hr	813	39.7	28.6	Select

(Clincalc, 2024)

- Bayesian method uses PK knowledge and patient data to predict AUC/MIC
- Bayesian-derived AUC monitoring allows early assessment without steady-state serum concentrations
- Bayesian estimation provides accurate AUC estimates with a single trough level before steady-state
- Effective as monitoring two levels at steady state

SUMMARY OF PRESENTATION

1. Vancomycin requires careful monitoring and administration to balance efficacy and minimise adverse effects.
2. Pharmacokinetic and pharmacodynamic characteristics vary among patients, necessitating individualised dosing for effective treatment.
3. Pharmacists play a crucial role in Antimicrobial Stewardship (AMS), ensuring optimal Vancomycin dosing based on PK/PD considerations.
4. AMS efforts are vital for maximising bacterial eradication and preventing resistance development.
5. SALHN guidelines for Vancomycin dosing can be ambiguous; consultation with infectious diseases or AMS pharmacists is recommended when uncertain.
6. Multidisciplinary collaboration (nurses, doctors, pharmacists) is essential for achieving optimal patient outcomes.
7. AUC/MIC ratio is pivotal for Vancomycin efficacy and minimising complications, particularly in serious MRSA infections or suspected toxicity early in therapy.
8. CALHN utilises AUC/MIC monitoring, but it has not been adopted in other SA Health hospitals yet.

QUESTIONS

Feedback and Advice

EVALUATION

Scan QR code

https://forms.gle/7y9GDJDPJuFw6TbK6

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Yusri Kardo is a resident clinical pharmacist at Mount Gambier Hospital and is enrolled in the SHPA/ANZCAP Residency program. He is currently undertaking a Graduate Certificate of Pharmacy at University of South Australia.

Yusri is committed to evidence-based practice and is currently working on his research project to assess compliance with institutional VTE Prophylaxis Therapy Guidelines to enhance quality use of medication. Furthermore through his work he hopes to educate colleagues, patients, nurse and allied health staff on the safe use of medicine.

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